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This opinion (1) was not written for publication and (2) is not binding precedent of the Board.

Paper No. 23

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOHN E. SHIVELY

Appeal No. 93-3623
Application 07/629,690

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and TORCZON, Administrative Patent Judges.

TORCZON, Administrative Patent Judge.

DECISION ON APPEAL

BACKGROUND

A. The nature of the case

1. This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1-15 and 19-25. No other claims are pending.

2. Appellant filed the subject application on 18 December 1990. He claims the benefit under 35 U.S.C. § 120 of the following United States patent applications: 07/174,956 (filed 29 March 1988, now United States patent 5,061,635, issued 29 October 1991), which was a continuation-in-part of 07/072,754 (filed 13 July 1987, now abandoned), which was a continuation-in-

part of 06/896,724 (filed 15 August 1986, now abandoned). The 07/072,754 application was the subject of Ex parte Shively, Appeal No. 90-2219 (Bd. Pat. App. & Inter. 27 Aug. 1990), affirmed, Appeal No. 91-1025 (Fed. Cir. 1991) (Fed. Cir. R. 36).

3. Appellant indicates (Paper 18 (App. Brief) at 3) that the Federal Circuit also reviewed his 06/896,724 application as part of a consolidated appeal. The record indicates that the Federal Circuit reviewed the 06/892,579 application, filed 1 August 1986, now abandoned. Ex parte Shively, Appeal No. 89-2337 (Bd. Pat. App. & Inter. 27 Aug. 1990), affirmed, Appeal No. 91-1024 (Fed. Cir. 1991) (Fed. Cir. R. 36). Appellant has not indicated a claim for the benefit of 06/892,579 application in the present application.

4. The present application is a divisional application from the 07/174,956 application. (Paper 2 (Req. Div. Appl'n.).) The resulting 5,061,635 patent has method, but not apparatus, claims.

5. The present application is entitled "Protein or peptide sequencing method and apparatus". The subject matter of the invention is reactors for peptide sequenators. (Paper 1 (Spec.) at 1.)

6. The claims on appeal broadly encompass three distinct embodiments. Claims 1, 9, and 19 illustrate the first (Fig. 1),

second (Fig. 10), and third (Figs. 11 & 12) major embodiments, respectively, that are at issue in this appeal:

> 1. A continuous flow reactor including a first tube for passing reactive fluids and solvents from a peptide sequenator into a reaction chamber packed with peptide coated discrete objects and a second tube for removal of solvents and reaction products from the reaction chamber which comprises:
>
> (A) a reaction chamber formed from a pliable, chemically inert tube; [and][1]
>
> (B) first and second pliable, chemically inert tubes for connecting the reaction chamber to a sequenator,
>
> (C) the inside and outside diameters of said reaction chamber tube and said first and second connecting tubes being so dimensioned that two leak-tight interference fit joints are provided by inserting one end section of a tube into the end section of another tube, one of said leak-tight interference fit joints being provided between said first tube and said reaction chamber and the other being provided between said second tube and said reaction chamber.
>
> 9. A continuous flow reactor for a peptide sequenator comprising:
>
> (A) a cylindrical reaction chamber formed from a pliable, chemically inert tube; [and][1]
>
> (B) first and second pliable, chemically inert tubes for connecting the cylindrical reaction chamber to a sequenator,
>
> (C) the inside and outside diameters of said cylindrical reaction chamber and said first and second connecting tubes being so dimensioned that two leak-tight interference

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[1] The bracketed items appear to be missing from the claims.

> fit joints are provided by inserting one end section of a tube into the end section of another tube, one of said leak-tight interference fit joints being provided between said first tube and said cylindrical reaction chamber and the other being provided between said second tube and said cylindrical reaction chamber[,][1]

said cylindrical reaction chamber containing at least one strip of hydrophobic membrane bearing a peptide sample, said strip being positioned in said cylindrical reaction chamber with its longitudinal axis substantially parallel to the longitudinal axis of said chamber.

19. A reactor for a protein or peptide sequenator comprising:

an elongated body member;

a longitudinal passage for the flow of fluids through said body member;

at least one end of said passage having a convex surface to receive a cap member having a concave outer surface;

the inner wall of a central portion of said passage being raised, whereby the diameter of said passage in said portion is reduced; and

shoulders at one end of said raised portion in said passage to abut the end of an inlet or outlet tube carried by said cap member.

7. Although Appellant states that claims 1-15, 19, and 20 are "the same or substantially the same as the claims at issue on the consolidated Federal Circuit appeals" (Paper 18 at 3), the second (claims 9-15) and third (claims 19 and 20) embodiments first appeared in his later 07/174,956 application. Applicant

added claims 21-25, which correspond to the first embodiment, by amendment to the present application. (Paper 5 (Amdt. B).)

B. The rejection

8. The examiner relied on statements about the prior art in the specification and the following references in rejecting the claims under 35 U.S.C. § 103 (Paper 16 (Final Rej.) at 2-7):

Winter et al. (Winter)	3,346,486	10 Oct. 1967
Hrdina	3,615,235	26 Oct. 1971
Johnson	4,180,383	25 Dec. 1979
Leaback	4,276,048	30 June 1981
Hara	4,289,620	15 Sep. 1981
Urdea et al. (Urdea)	4,483,964	20 Nov. 1984
Hood et al. (Hood)	4,603,114	29 July 1986

and

Aebersold et al., "Electroblotting onto Activated Glass", 261 J. Biol. Chem. 4229, 4230 (25 Mar. 1986) (Aebersold).

9. Specifically, the examiner rejected:

Claims	in view of	Combination
1-3, 6-8, and 21-25		Hrdina and Winter, Leaback, or Hara
4 and 5		Winter, Hrdina, Johnson, Leaback, Hara, and Hood
9, 10, and 12-15		Winter, Leaback, Hara, and Hood
11		Winter, Leaback, Hara, Hood, and Aebersold
19 and 20		Winter, Hrdina, and Hara
1-8 and 21-25		Urdea, admitted prior art, and Winter, Hrdina, Leaback, or Hara

10. The examiner has apparently withdrawn her rejection under 35 U.S.C. § 112 (Paper 16 at 2) in light of an after-final amendment (Paper 19 at 1). (Cf. Paper 21 (Ex. Ans.) at 2-3.)

11. Appellant argues the claims in the following groups: I - 1-3, 6-8, 21-25 (first embodiment); II - 4 and 5 (dependent from the first embodiment); III - 9-15 (second embodiment); and IV - 19 and 20 (third embodiment). (Paper 18 at 6.)

FINDINGS OF FACT

A. Protein sequencing

1. Claim 1 requires

A continuous flow reactor including a first tube for passing reactive fluids and solvents from a peptide sequenator into a reaction chamber . . . and a second tube for removal of solvents and reaction products from the reaction chamber which comprises:

(A) a reaction chamber formed from a pliable, chemically inert tube; [and]

(B) first and second pliable, chemically inert tubes for connecting the reaction chamber to a sequenator[.]

Hrdina

2. Hrdina's field of invention is a flow-through reactor that would be useful for amino acid analysis. (1:1-51.)

3. Appellant declares that "[t]he Hrdina reactor would not be practically useful for protein sequencing". (Decl. I at ¶ 20.)

4. Appellant knew, or should have known, based on a fair reading of Hrdina, particularly in view of the previous Board decision (Appeal No. 90-2219 at 4), that Hrdina is directed to reactors for amino acid analysis.

5. Although Appellant provides reasons why Hrdina's seals create problems, he also notes that Hrdina suggests omission of those seals. (Decl. I at ¶ 12(i).)

6. We find, on balance, that Appellant's declaration evidence is inconsistent with, and less credible than, the express teachings of Hrdina itself for understanding what Hrdina would have meant to a person having ordinary skill in the art.

7. We find that Hrdina is an appropriate reference in the field of Appellant's endeavor: continuous-flow reactors for protein or peptide analysis.

Urdea

8. Urdea teaches a reactor system for degrading linear polymers (Abstract), including proteins (3:39-46).

9. Appellant declares that "[t]he device, as disclosed in the Urdea patent, is not useful for the sequencing of proteins."

10. Appellant knew, or should have known, base on a fair reading of Urdea, that it teaches or suggests reactors for degradation of polypeptides.

11. Appellant provides no objective basis for us to evaluate his contention that "Urdea apparently was dismissed by persons skilled in the protein sequencing art." (Decl. I at ¶ 11(ii)(c).)

12. To the extent that Appellant is urging that Urdea is not an enabling reference (Decl. I at ¶ 11(ii)(c)), we note that patent disclosures are not required to be production specifications. Northern Telecom, Inc. v. Datapoint Corp., 908 F.2d 931, 941, 15 USPQ2d 1321, 1329 (Fed. Cir. 1990). We further note that patents are presumed to be enabling. 35 U.S.C. § 282. Appellant provides no objective evidence that one skilled in the art would not, at the time of his invention, have been able to analyze peptides using an apparatus suggested by Urdea's disclosure.

13. On balance, we find that Appellant's declaration evidence is inconsistent with, and less credible than, the

express teachings of Urdea itself for understanding what Urdea would have meant to a person having ordinary skill in the art.

14. We find that Urdea is an appropriate reference in the field of Appellant's endeavor: continuous-flow reactors for protein or peptide analysis.

15. We further find that, to the extent that either Hrdina or Urdea alone might not independently teach or suggest a continuous-flow reactor for protein or peptide sequencing, together they provide a foundational teaching in the field of continuous-flow reactors for protein or peptide analysis.

B. Leak-tight interference fit joints

16. Claim 1 further requires

> the inside and outside diameters of said reaction chamber tube and said first and second connecting tubes being so dimensioned that two leak-tight interference fit joints are provided by inserting one end section of a tube into the end section of another tube, one of said leak-tight interference fit joints being provided between said first tube and said reaction chamber and the other being provided between said second tube and said reaction chamber.

Appellant's disclosure

17. Appellant discloses that leak-proof joints are the result of interference or press fits between supply/drain tubes **12**/**16** and a reaction tube **14**, with a specified size relationship. (Paper 1 at 6.) The disclosed relationship is a 1:2 ratio in outer diameter, where the inner diameter of the reaction tube is almost as large the supply/drain tubes' outer diameter. (Paper 1

at 5-6.) The relationship between the drain and reactor tubes may be reversed to provide a "reaction zone free of unswept volumes". (Paper 1 at 6.)

18. Appellant discloses a reaction tube **14** with an inner diameter of 1/16 inch (approximately 1.6 mm). (Paper 1 at 5-6.)

Hrdina

19. Hrdina notes that an essential feature of the flow-through reactors of automated amino acid analyzers is a thin capillary tube, preferably made of polytetrafluoroethylene (PTFE, e.g., TEFLON®). (1:44-51.)

Urdea

20. Urdea uses a glass reactor, but notes that reactor structural material is not critical as long as it is inert. (4:44-46.)

21. Urdea further teaches that PTFE is inert and that it may be used for other components, including the tubes **26, 28** into and out of the reactor **12**. (5:50-60.)

22. We find that, taken as a whole, Urdea would have reasonably suggested an all-PTFE construction.

Leaback

23. Leaback teaches the use of a non-wettable (e.g., PTFE) inlet tube for an inert reaction chamber (1:66-2:12) for use in microvolume biochemical assays involving enzyme (protein) bearing substrates and related reactions (1:8-16 & 31-38).

24. We find Leaback's problem to be sufficiently related to the problem facing Appellant (microvolume sequencing of peptides) to be relevant to a person having ordinary skill in the art.

25. Leaback states that a wettable material for the reaction chamber is preferable (2:8-12), but also teaches that the chamber may be integrally formed with the inlet tube, suggesting that they may be formed of the same material. (2:45-48.) The outlet tube may be the same material as the inlet or reactor tubes. (2:36-39.)

26. We find that Leaback, taken as a whole, would have reasonably suggested an all-PTFE construction.

27. Leaback teaches that proper mixing and flow (and hence avoidance of unswept volumes) is, in part, a function of reactor diameter. (2:17-25.) It discloses a reactor with an inner diameter of approximately 1.6 mm. The inlet tube has half that inner diameter. (2:26-30.) The outlet tube may be coaxial with the reactor and the same size as the inlet tube. (2:33-39.)

28. We find that Leaback discloses the same structural and size relationship that Appellant is claiming, but the materials of the inlet and reactor tubes are different and their joint is secured with an adhesive. (6:14-27; Fig. 1.)

29. Leaback teaches the importance of fluid-tight seals in microvolume reactions. (2:48-53.)

Winter

30. We note that Winter teaches the desirability of fluid-tight joints (2:12-53) in an apparatus for the cyclical analysis of peptides (1:11-70).

Admitted prior art

31. Applicant's admitted prior art, specifically D.H. Hawke et al., "Microsequence Analysis of Peptides and Proteins", 147 Analytical Biochemistry 315, 329 (June 1985), "noting that Teflon[®] is 'self-sealing', report[s] lower background levels and increased yields deemed to be consequent from a better seal achieved in the all Teflon[®] design as compared to the seal observed with the Hewick glass cartridge." (Paper 1 at 2-3.)

32. We find that the admitted prior art would have provided the motivation to use the all-PTFE constructions suggested in the other references, and that a person having ordinary skill in the art would have understood that such a construction would have been "self-sealing", obviating the need for additional seals or adhesives.

33. We find that Appellant's declaration regarding his comparative data with Hawke and the "best prior art" (Decl. I at ¶¶ 9-11) unpersuasive. Appellant states that "the Teflon[®] version of the Hood cartridge reactor [used in Hawke] was the most advanced sequencer reactor extant [and] represents the best prior art available at the time the invention of claims 1-12 was

made." (Id. at ¶ 11(ii)(a), emphasis added.) The best extant design Appellant knows of is not necessarily the same thing as the closest prior art. In the present case, the closest prior art is a combination of the all-PTFE reactor elements with the cylindrical/capillary designs of Urdea/Hrdina/Leaback. The declarations do not address this combination. See In re Baxter Travenol Labs., 952 F.2d 388, 392, 21 USPQ2d 1281, 1285 (Fed. Cir. 1991) (Comparison must be with the closest configuration of the prior art).

Teachings of the art taken as a whole

34. We find that cited references and the admitted prior art, taken as a whole, would have provided motivation to a person having ordinary skill in the art to use an all-PTFE design to overcome any problems with seals between PTFE and non-PTFE components.

35. We further find that the resulting self-sealing PTFE joints would have been considered as leak-tight (Paper 1 at 2-3) and would obviate the need for washers, collars, adhesives, etc.

C. Discrete objects

36. Claim 1 requires "a reaction chamber packed with peptide coated discrete objects".

37. Claim 4 further requires that "the peptide coated discrete objects with which the reaction chamber is packed

comprise peptide coated porous silica objects." (Emphasis added.)

Hrdina

38. Hrdina teaches the use of porous, inert particles for packing the reactor of an amino acid analyzer. (2:27-35.)

Urdea

39. Urdea teaches the use of solid-phase supports for polypeptides in the reaction chamber, specifically beads or particles. Such supports should be porous and chemically inert. Urdea specifically teaches the use of silica beads (e.g., Fractosil®) as the preferred support. (4:60-5:9.)

Johnson

40. Alternatively, we further note the teachings of, e.g., Johnson that discrete, amorphous silica microparticles are a conventional support for peptides. (6:43-7:2.) Johnson also teaches coating the silica particulate substrate with protein. (7:28-39.) We recognize that Johnson is not directed to a peptide sequencing per se, but it is directed to selective binding and elution in a continuous-flow reactor and is thus sufficiently related to the problem facing the inventor to be instructive to a person having ordinary skill in the art.

41. We find that Appellant provides no basis for us to evaluate his declaration that Johnson is not analogous. (Decl. I at ¶ 12(ii).) As explained in the preceding paragraph, Johnson

meets at least the second, alternative, basis for finding analogousness. In re Deminski, 796 F.2d 436, 442, 230 USPQ 313, 315 (Fed. Cir. 1986). On balance, we find Appellant's conclusory statement to be unpersuasive.

Teachings of the art as a whole

42. We find that Urdea alone or in view of Hrdina or Johnson would have taught a person having ordinary skill in the art the use of peptide-coated discrete particles, preferably made of silica, as the solid-phase support in a reactor.

D. Longitudinal, hydrophobic membrane

43. Claim 9 (the second contested embodiment, Fig. 10) requires

> at least one strip of hydrophobic membrane bearing a peptide sample, said strip being positioned in said cylindrical reaction chamber with its longitudinal axis substantially parallel to the longitudinal axis of said chamber.

44. Hood is directed to an apparatus for the sequential degradation of peptides. (1:11-16.) It teaches the use of a solid matrix to support the sample. (7:16-26.) The matrix may be a thin film on the walls of the reaction chamber (Fig. 18A) or a porous sheet mounted transversely across the chamber (Fig. 6A). (7:27-33.)

45. Hood's thin-film embodiment is essentially longitudinal with the flow of reactants through the reaction chamber. (26:24-28.)

46. The porous sheet is made of a compressed fibrous material such as glass. (24:23-25.)

47. The record is not clear about whether porous glass would have been considered hydrophobic.

48. We find that Hood does not teach or suggest orienting the hydrophobic membrane longitudinally. Hood describes the porous sheet as a "filter". (24:25-28.) We find insufficient motivation to reorient Hood's transverse filter to become a longitudinal substrate.

49. The examiner has provided no guidance on, and we do not see, how Hara, Winter, and Leaback might supply the teachings or suggestions missing in Hood.

E. Contoured cap and passage

50. Independent claim 19 (the third contested embodiment, Figs. 11 & 12) requires

> at least one end of said passage having a convex surface to receive a cap member having a concave outer surface;
>
> the inner wall of a central portion of said passage being raised, whereby the diameter of said passage in said portion is reduced; and
>
> shoulders at one end of said raised portion in said passage to abut the end of an inlet or outlet tube carried by said cap member.

Hara

51. Hara teaches the use of a "column end fitting plug." (2:35-36.)

Winter

52. Winter teaches threaded plugs **34** & **42**. (2:29-32 & 45-47.)

Hrdina

53. Hrdina does not add any relevant teachings or suggestions directed to the excerpted limitations.

The teachings of the art as a whole

54. We find that Hrdina, Winter, and Hara do not provide sufficient guidance from which a person having ordinary skill in the art could reasonably "determine the most appropriate cap attachment means" (Paper 21 at 12) and come up with the structural features recited in claim 19.

F. Additional findings

55. We find, based on the references, most of which are assigned to, or otherwise appear to originate from, academic research institutions, that the level of skill in the art is quite high. In re GPAC Inc., 57 F.3d 1573, 1579, 35 USPQ2d 1116, 1121 (Fed. Cir. 1995).

56. To the extent that Appellant is urging that his results are unexpectedly good, we find that his arguments and evidence of record neither substantially support that finding nor

specifically urge that finding with regard to the closest prior art. In re Geisler, 116 F.3d 1465, 1470-71, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997).

CONCLUSIONS OF LAW

A. Weight of evidence

1. A conclusion of obviousness must be based on a preponderance of evidence, with due consideration for the weight of the evidence and the persuasiveness of the argument. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

2. Declaration evidence must be evaluated as part of the totality of evidence. Baxter Int'l Inc. v. Cobe Labs., 88 F.3d 1054, 1058, 39 USPQ2d 1437, 1441 (Fed. Cir. 1996). Declarations unsupported by objective evidence may be accorded little or no weight. In re Etter, 756 F.2d 852, 860, 225 USPQ 1, 6 (Fed. Cir. 1985). A declaration and its support must be relevant to the question at hand. Schendel v. Curtis, 83 F.3d 1399, 1403, 38 USPQ2d 1743, 1746 (Fed. Cir. 1996)

3. The relationship between the declarant and the inventor is relevant in determining the weight to be accorded the affidavit. Refac Int'l, Ltd. v. Lotus Dev. Corp., 81 F.3d 1576, 1581-82, 38 USPQ2d 1665, 1669 (Fed. Cir. 1996). Indeed, an inventor is presumed to support the patentability of the claimed invention to the extent that the absence of favorable inventor

testimony, in some circumstances, may even be counted against the inventor. Borror v. Herz, 666 F.2d 569, 573-74, 213 USPQ 19, 23 (CCPA 1981).

4. Appellant's "opinion" concluding that omission of the seals from Hrdina would not, by itself, have rendered the claims 1-12 (and presumably 13-15 and 21-25) obvious, is not a proper use of fact testimony. E.g., In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991) (dismissing unsupported "expert opinion" on an ultimate issue).

5. Appellant's analysis of the separate deficiencies of each reference (see, e.g., the preceding paragraph) and the admitted prior art is not proper approach to contesting an obviousness rejection involving a combination of references. In re Merck & Co., 800 F.2d 1091, 1097, 231 USPQ 375, 380 (Fed. Cir. 1986).

6. The examiner must be careful in relying on ordinary skill in the art to arrive at specific limitations in the absence of some teaching or suggestion at least implicit in the art of record. Otherwise, as with claims 9-15, 19 and 20, the rejection will appear to depend on improper hindsight. W.L. Gore & Assocs. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983).

B. Analogousness

7. To be relevant in an obviousness rejection, a reference must either be in the field of the applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned. In re Deminski, 796 F.2d 436, 442, 230 USPQ 313, 315 (Fed. Cir. 1986). Thus, it is not sufficient for Appellant to observe that a reference is not directed to peptide sequencing (even where the observation is true), when all of the references are directed to microvolume analysis of biochemicals in a reactor, generally involving peptides and substrates. Prior art is relevant for all it fairly teaches even if directed to a somewhat different problem. In re Napier, 55 F.3d 610, 614, 34 USPQ2d 1782, 1785 (Fed. Cir. 1995).

C. Claim interpretation

8. We must interpret claims as broadly as their terms reasonably allow in light of the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

9. Claim 1 does not exclude the additional use of adhesives, plugs, or seals to secure the interference fit.

10. Claim 1 does not require the reactor to be free of unswept volumes. Both the specification (Paper 1 at 6) and dependent claim 8 associate this advantage with a specific arrangement. Cf. 35 U.S.C. § 112[4] (requiring dependent claims to specify a further limitation of the claimed subject matter).

11. Patentability cannot be predicated on unclaimed features. In re Schreiber, 128 F.3d 1473, 1479, 44 USPQ2d 1429, 1433 (Fed. Cir. 1997).

D. Obviousness

12. After considering the combined teachings of the admitted prior art, Urdea, and Hara, Winter, Hrdina, or Leaback, we conclude that the subject matter of claims 1 and 4, representing Appellant's separately argued groups I and II, would have been obvious to a person having ordinary skill in the art at the time of Appellant's invention. Thus, we affirm the examiner's sixth rejection covering claims 1-8 and 21-25.

13. In light of our conclusion regarding the sixth rejection, we need not reach the first and second rejections covering the same claims. We note, however, our reliance on the admitted prior in reaching our conclusion.

14. We conclude that claims 9-15 would not have been obvious based on Hood, Hara, Winter, and Leaback. Consequently, we reverse the examiner's third and fourth rejections.

15. We conclude that claims 19 and 20 would not have been obvious based on Hrdina, Winter and Hara. We, therefore, reverse the examiner's fifth rejection.

DECISION

We affirm the rejection of claims 1-8 and 21-25. We reverse the rejections of claims 9-15, 19 and 20.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a). See 37 CFR § 1.136(b).

AFFIRMED-IN-PART

SHERMAN D. WINTERS Administrative Patent Judge	)
WILLIAM F. SMITH Administrative Patent Judge	) BOARD OF PATENT APPEALS AND INTERFERENCES
RICHARD TORCZON Administrative Patent Judge	)

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